

OBSERVATIONS ON MODERN METHODS IN THE
TREATMENT OF DIABETES MELLITUS.

1923
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INTRODUCTION.

When we review the various methods which have been suggested for the treatment of diabetes mellitus we find that for many years very little of importance was contributed to this branch of medicine.

As we shall see later the subsequent progress in the elucidation and treatment of this disorder of metabolism depended on the accurate knowledge of of the histology of the pancreas, the recognition of the rôle of the internal secretions, and the perfection of physiological chemical methods.

Whereas the presence of sugar in the urine was at onetime considered evidence of true diabetes, we know now that this is compatible with a state of abnormally low sugar content in the blood i.e. Hypoglycaemia. On the other hand in true diabetes there is always a Hyperglycaemia or excessive amount of sugar in the blood.

During the past thirty years new medicinal methods of treatment have been put forward by different authorities, only to be discarded eventually as worthless; and up to the present the significant advances consisted in the elaboration of dietetic and hygienic measures.



Generally speaking the drugs which have been vaunted from time to time have proved useless except as placebos. On the other hand attention to a carefully regulated dietary and hygienic regime served often to control the course of the disease and prevent complications.

Recently some very important researches have been made in reference to a new line of treatment by two Canadian physiologists Banting and Best. It is the object of the author of this thesis to give a brief account of the various developments in connection with the treatment of diabetes, which led to the discovery of the Insulin treatment by Banting and Best.

HISTORICAL OUTLINE.

The recognition of Diabetes Mellitus dates back to very early times, but descriptions are vague and incomplete. In that Egyptian compilation known as the Ebers Papyrus (about B.C. 1500.) there is mention of polyuria.¹ The condition was evidently known to the Hindus judging from some passages of the Ayur Veda about (A.D. 500.) According to Berdoe² (Origin and Growth of the Healing Art [London 1893] Demetrius of Apamea (B.C. 276) named and described Diabetes. Celsus (B.C. 50- A.D. 7) refers to an inordinate increase of the urine leading to emaciation and endangering life (Lib 4 Cap 20 Para 2).

Aretaeus of Cappadocia (1st century) explains the etymology of diabetes; namely, the transudation (*διαβαίνειν*), of the liquid constituents of the body into the urine, and attributed the disease

to disorder of the stomach.

(De causis diut. lib 2 cap 2 De morb. diut. curat. lib 2 cap 2.)

Galen. (b.A.D.170) believed that the diuresis was a disease of the kidneys which attracted to themselves the fluids drunk and excreted them unchanged (De loc affect. lib 4 cap 3). Almost all the later physicians of antiquity and of the middle ages, and even later, held this view of Galen's; with the exception of a few who maintained Aretaeus' theory of an original affection of the stomach.

Paracelsus (1493 - 1541) on the other hand attributed the disease to an abnormal formation of salt in the body, whereby the kidneys were stimulated to greater activity (De tartaro lib 2 tract 3 cap 1)

Sylvius (1614 - 1672) regarded Diabetes as a result of a morbid condition of the blood.

(Opera med Amstelodami 1680 p.724).

Thomas Willis 1621 - 1675) the English physician mentions the fact that the urine in this disease has a sweet taste (Pharmacent ration. Oxford 1674).

Matthaeus Dobson also an Englishman demonstrated the presence of sugar in diabetic urine.

(Medical observations by a Society of physicians in London 1775).

John Rollo another English physician maintained that vegetable food was injurious, being converted into sugar by an abnormal gastric secretion. He accordingly introduced the absolute meat diet into the treatment of Diabetes.²⁷

Claude Bernard (1813 - 1878) demonstrated the relation of the liver to sugar formation, and produced glycosuria experimentally by puncture of the medulla oblongata. The experimental work of Claude Bernard marked a new epoch in the study of Diabetes, and gave a new impetus to the search for the pathogenesis of the disease.

(Nouvelles fonctions du foie considerée comme l'organe producteur de matiere sucre - Paris 1853 Lecons de physiologie experimentale appliquee a la medecine Paris 1854 - 1855).

Bernard maintained that the liver normally forms sugar or a substance readily convertible into it, now termed glycogen. Carbohydrates are first hydrated in the alimentary canal to form sugar, this passes to the liver where it is dehydrated to form glycogen, and subsequently hydrated once more to pass to the tissues as sugar, where it undergoes combustion.

In Diabetes the glycogenic function is upset, and excess of sugar passes into the blood leaving the body in the urine. Bernard believed that this is due to an increased formation of sugar from glycogen.

Pavy on the other hand denies that the liver is a sugar-forming organ; he maintains that the excess of sugar in the blood is due to the diminished formation of glycogen from the sugar of the portal blood.²³

Cohnheim's view as to Carbohydrate metabolism is interesting.

He holds that the sugar of the blood is burnt up in the muscles through the agency of a substance produced by the interactions of bodies

originating in the pancreas and muscles.

This view has been corroborated by recent experiments of Knowlton and Starling.

They showed that the consumption of sugar by the diabetic heart was much below that of the normal heart, and further that this loss of power to utilise sugar in the diabetic heart, was due to the absence of some substance normally present in the heart and circulating blood, and presumably formed by the pancreas.

It was ¹⁴ Lancereaux in 1877 who suggested that glycosuria was intimately associated with pronounced alterations in the structure of the pancreas. (Notes et réflexions sur un cas de Diabete sucré avec alteration du Pancreas- Bull. de l'Acad. de med Paris 1877 ~~serie~~ 2 tome 6 p 588)

The connection between the two conditions was subsequently established by the experiments of ¹⁷ Merling and Minkowski. (Diabetes Mellitus nach der Extirpation des Pancreas - Arch. f. Exp. Pathologie Bd. 26 1889).

THE EVOLUTION OF THE STARVATION TREATMENT OF ALLEN.

Allen removed various fractions of the pancreas from dogs and found that when only a sixth was left the dog died rapidly with many of the symptoms and signs of diabetes mellitus.

If the dog were starved for a time the sugar disappeared from the urine and then if the diet were regulated very carefully, the glycosuria remained

absent and the animal could be kept alive indefinitely, As long as the lowest possible diet necessary for the needs of the animal was given, the animal would be healthy, but when this was exceeded no matter what the nature of the food was, diabetes would follow.

It is not enough to restrict the carbohydrates the other foods, proteids, and fats must also be cut down.

Drawing an analogy between these partially pancreated dogs and human diabetics, Allen concluded that the proper treatment for diabetes should consist in giving the patient the least amount of food necessary for the requirements of the body. Such is the basis of the modern treatment of diabetes.²

ABNORMAL METABOLISM IN DIABETES.

In the normal state glucose does not accumulate in the blood; the proportion of glucose in the blood remains constant at a figure between 0.09 and 0.11%. This state of affairs seems to depend on a harmonious physiological process in which the pancreas, nervous system, and such glands as the thyroid and suprarenals all take part. In normal health the glycogen of the liver is derived from the carbohydrates contained in the food.

During fasting the hepatic and muscular glycogen becomes exhausted, and the blood will always contain the same amount of glucose resulting from the transformation of albumins and fats of the organism.

There are three processes capable of furnishing the body with glucose, firstly, the transformation

of the carbohydrates of the food, secondly, the transformation of the albumins and fats of the food, and thirdly, the transformation of the albumins and fats of the tissues of the organism.

The first is normal the second is abnormal, and the third is still more abnormal.

When the organism has its choice it is probable that it only utilises the first process, and it must be forced by abnormal circumstances to put into effect the second and above all the third process.

Normally no matter what may be the amount of the carbohydrate intake or the rapidity with which carbohydrate enters the circulation, the liver and muscles retain them in the form of glycogen, and the tissues burn them up completely, so that neither hyperglycaemia nor glycosuria develops.

In the pathologic state things are different. As soon as a disturbance arises in the sugar - regulating mechanism, the result of a morbid change in one of the organs composing this system, the carbohydrate metabolism no longer takes place with regularity, glucose is not carbonised completely by the tissues and consequently accumulates in the blood and tissues, giving rise to hyperglycaemia and glycosuria.

In Diabetes there are three characteristic derangements of metabolism, firstly, disturbance of the sugar regulating mechanism, secondly, disturbances of nitrogenous and fat metabolism and thirdly, acidosis. ^{2/} Von Noorden pointed out the necessity of determining the carbohydrate tolerance in every case of Diabetes,

that is the capacity for burning carbohydrates.

Patients vary greatly in their carbohydrate tolerance and as the latter indicates the degree of disturbance of the sugar-regulating mechanism, it will be seen how important it is to determine the extent of this tolerance, from the point of view of prognosis and treatment.

All starchy food taken in, is broken up in the intestine and absorbed as sugar, which passes by the portal vein to the liver, where it is stored as glycogen. When sugar is required by the muscles and other tissues this glycogen is transformed into glucose and transported to the tissues where it ^{is} oxidised and ultimately splits up into carbon dioxide and water.

In Diabetes a large proportion of this sugar instead of being used in the body appears in the urine.

Normally fat gets decomposed into oxybutyric acid, diacetic acid and acetone, which are ultimately split up into carbon dioxide and water, just as in the case of sugar. In Diabetes this final oxidation does not occur, and the intermediate products or Ketone bodies referred to, accumulate in the blood, producing a state of acid intoxication known by the name of acidosis.

Since acidosis is the precursor of the dangerous state of Coma, it is of the utmost importance to test the urine for acetone and diacetic acid.

Protein circulates in the blood as amino-acids produced by hydrolysis in the intestine, and these different acids are picked up by the various tissues according to their needs. When the nitrogenous waste of the

tissues is supplied the remaining acids undergo a process whereby the nitrogen is removed, and this nitrogen is eliminated from the body as urea. The amino-acid minus nitrogen now joins either the carbohydrate or the fat path.¹⁸

Benedict and Joslin estimated the amount of nitrogen in the urine of diabetics and normal individuals during fasting and noted the comparative nitrogen excretion per Kilo of body weight and per hour.

In normal subjects they found an average excretion of 685 milligrams, in mild diabetics 870, and in serious diabetics 960. These researches show that diabetics metabolise proportionately more albumin than healthy subjects and that this exaggeration of nitrogenous metabolism is more pronounced, the more serious the diabetes.

Thus it will be seen that Diabetes is a disease of general metabolism in which all the ordinary kinds of food are involved; and it is on the recognition of this fact that the modern treatment is founded.

THE EVOLUTION OF THE "INSULIN" TREATMENT.

In 1889 Mering and Minkowski produced severe and fatal diabetes by total removal of the pancreas in dogs. They also showed that one fourth to one fifth of the gland left behind was sufficient to prevent glycosuria. Since then, the following experiments have been done; the pancreas has been completely removed from its normal connections without resulting glycosuria, a portion of the pancreas having been grafted elsewhere in the abdominal cavity or even under the skin. In addition the ducts of the gland may be completely

occluded by ligature or by injection of paraffin without causing glycosuria.

These experiments led us to believe that the pancreas forms an internal secretion which passes into the blood and plays an essential part in the metabolism of sugar in the body. The tissue concerned in this important function is not the pancreatic tissue proper but that composing the so called islets of Langerhans. Observers accordingly began to try the effects of feeding pancreas and giving injections of pancreatic substance in Diabetes.

X Minkowski, Sandmyer, Pfluger and others found that feeding with pancreas was followed by negative or harmful results. Murlin, Kleiner and Paulesco tried the effect of Aqueous Extracts of Pancreas intravenously on de-pancreatized animals and found a transitory reduction in the blood sugar.

X In 1907 Rennie and Fraser secured tissue from the islets of Langerhans in certain fishes and fed human diabetics, without beneficial results.

26.

In 1908 Zuelzer and his associates reported their results in the treatment of six cases of Diabetes Mellitus with a pancreatic extract obtained by expressing the juice from the pancreas, treating it with alcohol and evaporating the filtrate to dryness. The residue which contained the active principle of the pancreas was re-dissolved in salt solution or water and given by injection.

Following the intravenous injection of this extract in five diabetic patients kept on a fairly

constant diet the excretion of acetone, diacetic acid and sugar in the urine decreased or entirely disappeared. An improvement in the general condition of all patients treated was observed following the injection.

In four cases the excretion of acetone, diacetic acid and sugar in the urine returned to the former level in from one to four days after extract treatment was discontinued. The fifth case which was complicated by a large carbuncle was treated by incision of the carbuncle and by the extract. After the wound healed the urine of this patient remained free of sugar and acetone upon dietetic treatment alone. The intravenous injection of the extract in these five cases was accompanied by severe chills, fever and occasionally vomiting.

¹²
In 1909 Forschbach working in Minkowski's clinic reported his results in the treatment of two cases of Diabetes Mellitus with the Zuelzer extract which he obtained from the Schering Company of Berlin. In one case no effect was observed, in the other the administration of the extract, which was accompanied by chills and fever, reduced the excretion of sugar to one-fifth for a period of forty-eight hours. The positive effect in one case is attributed to the use of a freshly prepared extract. Owing to the severe toxic reaction following its administration the extract prepared by Zuelzer did not come into general use in the treatment of Diabetes Mellitus.

^{5,6,7.}
Banting and Best of the Physiological Department Toronto have worked on the subject.

First they attempted to eliminate the enzymes which they believed to be present in Pancreatic Extract and which destroyed the active principle. It was found that the acinous tissue of the Pancreas (from which the enzymes are derived) degenerates in 7 - 10 weeks after ligation of the Pancreatic Duct.

The Acinoustissue however survives. If the Pancreatic Ducts were ligatured, dogs did not become diabetic and only the acinous cells of the gland degenerated. The Ducts were therefore ligatured, and ten weeks later the degenerated pancreas was removed and extracted with saline.

It was observed that in a depancreatized dog the blood sugar rose 20 - 40 per cent in a few days, the animal became progressively weaker, developed great hunger and thirst, and lost flesh rapidly.

The injection of the pancreatic extract into such a dog caused a fall in the blood sugar, the animal became stronger and lost its ravenous appetite. This however was not a suitable method of preparing insulin. The long continued injection of secretin with the object of exhausting the acinous cells and thereby destroying trypsin was found to be unreliable. Later it was found that the Pancreas of foetal calves of under five months development did not contain proteolytic enzymes; the acinous cells containing no trypsin granules. (cf Ibrahim["] Brochen Leitschrift 1909 22 pp24-35).

Such foetal pancreatic extract was found to be very potent in lowering the blood sugar and the second

dog was killed by an overdose, and died with symptoms which are now known to be those of hypoglycaemia. The difficulty consisted in extracting the internal secretion from the whole pancreas by some chemical method which would destroy the proteolytic ferment and preserve the insulin in an active form.

Dr Cobb succeeded in fractionating out the active principle with 82% alcohol. Since then the process had been improved upon and insulin now contained no protein, was non-irritating, and more easily standardized.

Insulin in proper doses in the laboratory reduced the blood sugar to normal or less, it rendered the urine sugar free, and by its means a depancreatized dog could be kept alive at least three times as long as without it. Without insulin such a dog would live from eight to twenty days.

Dr Banting with insulin had kept a dog alive for seventy days; the animal was then killed and no islet tissue was found.

The liver of a depancreatized dog did not contain more than 0.5% of glycogen, but after insulin and glucose as much as 18 percent of glycogen might be present; insulin therefore enabled the dog to store glycogen in the liver.

Fat replaced glycogen in the liver of depancreatized dogs. Four days after the operation the liver might contain 11 to 12 percent of fat and no glycogen, whilst four days treatment with insulin might lead to the disappearance of fat, and the appear-

ance of 12 to 15 per cent of glycogen. Adequate doses of insulin would control all forms of hyperglycaemia.

The effects of overdose as seen in a rabbit accompanying the fall in blood sugar were hunger, the animal chewing the woodwork of its cage, it then became dull, had periods of intermittent convulsions and unconsciousness followed by coma. If given glucose the symptoms were relieved or prevented.

Banting Best, Collip Macleod and Noble (American Journal of Physiology November 1922 p 559), described the effects of Insulin on experimental hyperglycaemia in rabbits. The hyperglycaemia was produced in various ways.

viz, piqûre
 injection of epinephrin
 mechanical asphyxia
 carbon monoxide poisoning
 Ether.

In a rabbit previously inoculated with Insulin piquê failed to produce hyperglycaemia. It was also found that Insulin was capable of greatly reducing the hyperglycaemia, caused by epinephrin, provided the latter was not given in massive doses.

The same applied to rabbits in whom hyperglycaemia was produced by mechanical asphyxia, CO and ether poisoning.

Two perfectly distinct types of secreting cells are present in the pancreas, the one composing the secreting acini, the other collected into irregularly distributed groups which are more or less oval in shape and which vary in size in different species.

These are known as the " islets of Langerhans", and on account of their abundant blood and nerve supply, and the fact that the cells which compose them stain indifferently with any kind of stain while those composing the acini stain readily, many anatomists have considered them as quite independent of the acinar cells.

Others believe however, that the one kind of cell may change into the other, for example that the insular cells are nothing more than completely exhausted acinar cells. When secretin is repeatedly injected so as to exhaust the gland, it has been found by Dale¹⁰ that the acinar cells lose their power to stain, and come to be indistinguishable from the cells of the islets. The islets therefore look as if they were incorporating the acini themselves, and the whole picture gives the impression that islet cells are merely stages in the life history of the secreting cells.

The present day view of the commonest cause of Diabetes Mellitus is a degeneration of the "islets of Langerhans". Although the changes in the pancreas are not macroscopic as a rule, careful microscopic examination shows hydropic changes in some of the non-acinary cells.

CASE 1.

Mrs. C. aged 48, fairly well nourished, height 5ft 8ins., weight 11st.6lbs., first complained of thirst, polyuria and weakness in February 1923. Heart and Lungs normal. Menopause setting in.

The patient was very neurotic and after being told she had sugar became extremely hysterical and sent for me in the middle of the night. She was always a hearty feeder, and took a large quantity of bread and potatoes.

Urine. Amount in 24 hours 7 pints, Sp. gr. 1030.

Reaction Acid

Sugar 2%

Acetone None (Lieben's test KOH -Lugol's Iodine)

Diacetic Acid None (Gerhardt's test Ferric Chloride)

I decided to give the patient the "Allen" treatment.

In the first place the patient was put to bed and kept very quiet, the bowels were thoroughly cleared out by an enema, and afterwards a seidlitz powder was given daily the first thing in the morning.

The diet was as follows :-

<u>Breakfast</u>	240cc. (8ozs) weak coffee.
	300cc. (10ozs) beef tea.
<u>Lunch</u>	Same.
<u>Tea.</u>	240cc. (8ozs) weak tea.
<u>Dinner.</u>	240cc. (8ozs) weak tea.
	300cc. (10ozs) or more beef tea.

CASE 1 contd.

At bedtime

Potassii Bromidum gr.20.

Whisky 30cc. (1oz) well diluted

were given as the patient complained of weakness and sleeplessness.

At the end of the first day the amount of sugar in the urine was 1.5%, no acetone or diacetic acid. At the end of the second day sugar was 1%. On the third and fourth days 2 eggs and 8ozs. French beans were added to the dietary; sugar now $\frac{1}{2}\%$. On the fifth and sixth days fasting was resumed, and the sugar was now absent.

The patient was now put on a vegetable diet to determine the carbohydrate tolerance as follows:-

Seventh day:

Cabbage 6ozs - 6grams CH

Lettuce 4ozs - 4 " "

2 Bran Biscuits

Total 10 " " -

- 40 Calories.

Eighth day:

Cabbage 6ozs - 6grams CH

Spinach 4ozs - 4grams "

Lettuce 6ozs - 6 " "

Tomatoes 4ozs - 4 grams CH

2 Bran Biscuits

Total 20 grams CH - 80 Calories.

Ninth day:

Cabbage 8ozs - 8 grams CH

Lettuce 6ozs - 6 grams "

Orange 3ozs - 9 " "

Tomatoes 7oz - 7 " "

2 Bran Biscuits

CASE 1 contd.

Ninth day: Total 30 grams CH - 120 Calories.

Tenth day: Cabbage 8ozs- 8 grams CH

Lettuce 6ozs- 6 " "

Tomato 7ozs- 7 " "

Orange 5ozs-15 " "

Apple 2ozs 8 " "

Banana 1oz 6 " "

2 Bran Biscuits

Total 50 grams CH - 200Calories

Eleventh day: Cabbage 8ozs- 8 grams CH

Lettuce 6ozs- 6 grams "

Tomato 8ozs- 8 " "

Orange 8ozs-24 " "

Apple 6ozs-24 " "

2 Bran Biscuits

Total 70 grams CH - 280 Calories.

Twelfth day: Cabbage 8ozs - 8 grams CH

Lettuce 8ozs - 8 " "

Tomato 8ozs - 8 " "

Orange 8ozs -24 " "

Oatmeal $1\frac{1}{2}$ ozs-30 " "

Milk 4ozs - 6 " "

White bread 1oz-15 " "

2 Bran Biscuits

Total 99 say 100 $\frac{\text{grams CH}}{\text{Calories}}$ = 400+proteid &
fat = 510 Calories.

Thirteenth day: Cabbage 6ozs - 6 grams CH

Lettuce 6ozs - 6 " "

Tomato 6ozs - 6 " "

Apple 4ozs - 16 " "

Oatmeal 2ozs - 40 " "

Milk 6ozs - 9 " "

Bread 2ozs - 30 " "

Total 113 say 120 - 480 -

proteid & fat - 600 Calories.

At the end of the thirteenth day sugar began to appear in the urine. The patient was accordingly fasted again for 48 hours at the end of which time the urine was free from sugar, that is the 15th day.

Now we know that about a quarter of the total carbohydrates tolerated can be taken when protein and fat are included, therefore she would tolerate $\frac{100}{4}$ 25grams of carbohydrate when protein and fat are added.

For a period of 15 days after the urine was found free from sugar, Dr Leyton's tables were followed the amount of foodstuffs being multiplied by $\frac{10}{7}$ i.e. the ratio of the patients weight 160 to 112. At the end of the month the urine was free from sugar. I advised the patient to fast one day a fortnight, and the urine has been examined periodically and no trace of sugar found. A blood sugar test was made after the treatment with the following results:-

Initial - .106 %

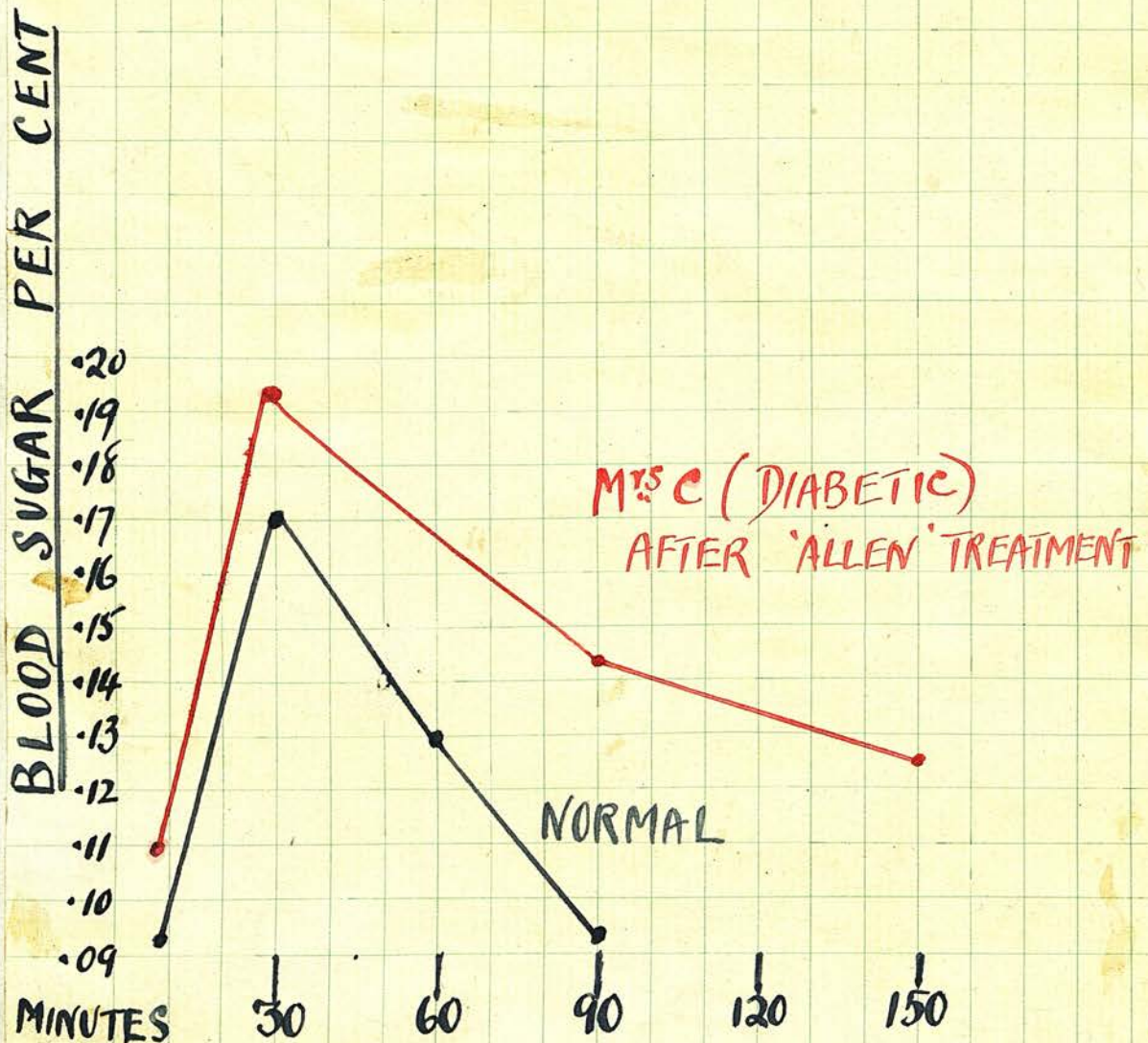
30 minutes after 50 grams of glucose - .193 %

90 " " " " " " - .143 %

150 " " " " " " - .125 %

CHART I.

20.



From the chart it will be seen that the blood-sugar curve indicates deficient storage capacity, and a distinct deviation from the normal curve with which it should be contrasted. Although there is no sugar in the urine the patient in my opinion ^{must} be regarded as a virtual diabetic.

CASE 2.

Mrs. F.L. aged 52, Height 5ft 2ins, Weight 9st. Consulted me in April 1923 on account of failing vision, great thirst, severe pains in the legs, and pruritus. Heart and Lungs normal, arteries atheromatous. Bloodpressure Systolic 180 diastolic 140.

Urine Amount in 24 hours 6 pints.

Sp. gr. 1035

Sugar 3 %

Albumin .6 % (Esbach's method)

Lieben's test for acetone ... positive

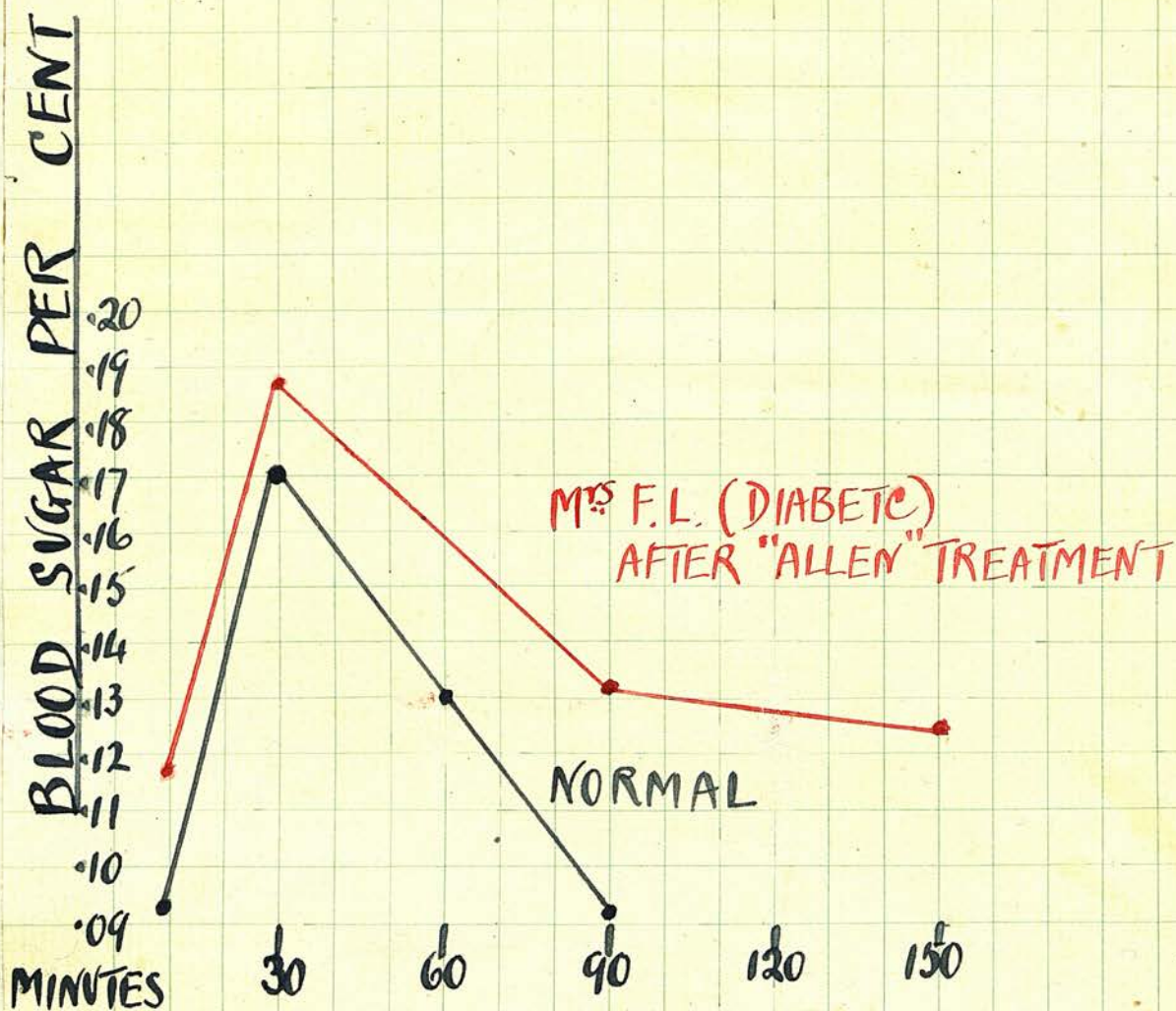
Gerhardt's test for Diacetic Acid positive.

Ophthalmoscopic examination revealed a streaky condition of both lenses (incipient cataract), tortuous retinal vessels with small flame shaped hemorrhages.

The patient was put on the "Allen" treatment and improved considerably. Three fasts were required to make the urine sugar free. The carbohydrate tolerance was 50 grams.

After two months rest and dietetic treatment, she felt much better, was not thirsty, and the pains in the legs disappeared. The urine was examined regularly, but sugar was always present, the smallest amount being $\frac{1}{2}$ %, there was no acetone or diacetic acid

^{22.}
CHART 2.



CASE 2 contd.

slight albuminuria persisted.

A blood sugar test was made with the following result, after the treatment;-

Initial	-	.118 %
30 minutes after 50 grams of glucose	-	.187%
90 " " " " " "	-	.131%
150 " " " " " "	-	.125%

The chart in this case indicates prolongation of the blood sugar curve and failure to come down to the original level after $2\frac{1}{2}$ hours; this patient is undoubtedly a diabetic but seems to react well to treatment.

CASE 3.

Mr M aged 53. Dealer in fancy goods:

Height 5ft 4 $\frac{1}{2}$ ins, Weight 11st 11lbs.

Sugar first discovered in January 1923.

The patient had been operated by Sir Kennedy Dalziel for stone in the bladder.

Urine in January

Amount 10 pints.

Sp. gr. 1040

Sugar 5 % -

Albumin traces.

Acetone and diacetic acid present.

As this patient would not rest and undergo a strict course of "Allen" treatment he was kept on the following diet for a considerable time:-

Breakfast; Tea or Coffee no sugar may use

CASE 3 contd.Breakfast: Saccharine.Brown or White Bread $\frac{1}{2}$ oz.

* Restricted
Diet. } Butter $\frac{1}{2}$ oz. Fish 4 oz. or more if
 desired Eggs 2 or meat 1 lean chop.
 Thin cream 1 oz.

Lunch: Bovril ordinary a large cup. Mutton
 4 ozs or more. Green Vegetables or
 Turnips after cooking 10 ozs (vegetables
 must be boiled in three different waters
 then squeezed and some butter is added)
 1 raw lettuce or two raw tomatoes.

Tea: Tea or Coffee 2 eggs Cheddar cheese
 1 oz. Butter $\frac{1}{2}$ oz. Thin cream 1 oz.
 Special Diabetic Bread or Biscuits.

Supper: Bovril 10 ozs.
 Chicken or Meat 4 ozs or more.
 Boiled Potato 2 ozs. Green vegetables
 10 ozs.

In addition I advised a seidlitz powder every
 morning, and frequent warm baths.

The patient complained of great lassitude,
 intense thirst, a ravenous appetite, somnolence almost
 amounting to narcolepsy, and neuritis of the right
 arm. The urine was examined fortnightly for 6 months
 but the sugar never fell below 3.5 %, acetone and
 diacetic acid were always present, and traces of
 albumin persisted.

In the first place I made a blood sugar analysis
 The method I have been using is Maclean's, and appar-

CASE 3 contd

atus by Allen & Hanbury which are most suitable for the general practitioner.

Blood sugar readings:

Initial	-	.312 %
30 minutes after 50 gms Glucose	-	.424 %
90 " " " " "	-	.38 %
150 " " " " "	-	.35 %

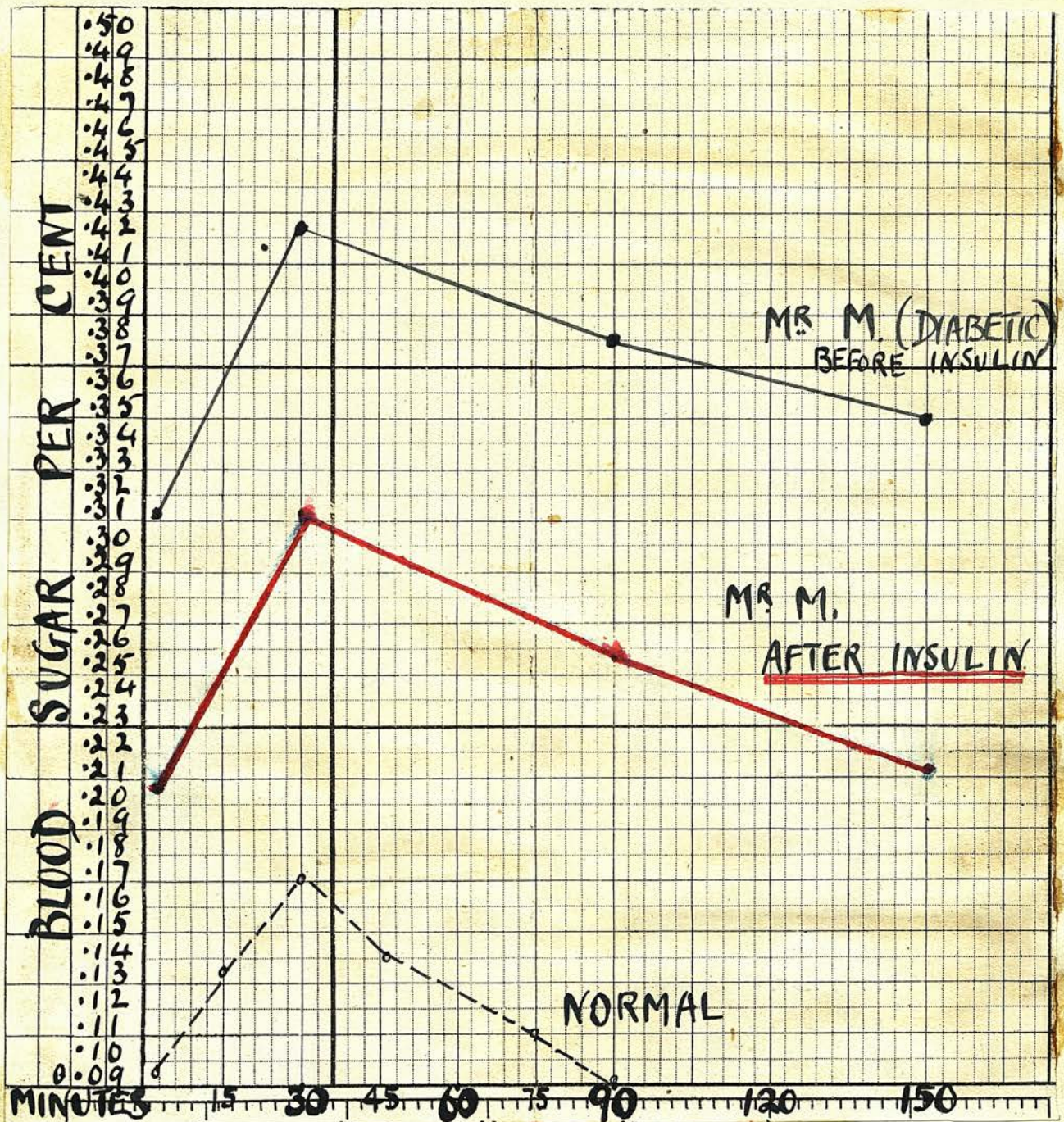
These figures pointed to the case being a true Diabetes of severe type. The first analysis shows a very high percentage of sugar, and even in $2\frac{1}{2}$ hours, the blood sugar had not fallen to the level of the first analysis (see chart). I kept the patient on the same restricted diet and injected .5c.c. Insulin i.e. 10 units subcutaneously $\frac{1}{2}$ an hour before the morning and evening meals, and examined the urine daily.

The Insulin I use is made by Allen & Hanbury and British Drug Houses.

For the first three days after Insulin treatment was begun, there was no appreciable difference in the state of the urine, but the patient said he felt more comfortable and was not so thirsty. On the 4th day there was pronounced diminution in the percentage of sugar in the urine viz 1.5 % and there was no acetone or diacetic acid.

A week after the Insulin treatment was commenced the patient declared "he never felt better in his life," his mind was active, and drowsiness during the day entirely disappeared, and the pain in his arm became much easier. The sugar in the urine however never

CHART 3.



CASE 3 contd.

entirely disappeared but at the end of a fortnight's treatment was only $\frac{1}{2}$ %.

Another blood sugar test was now made and the figure was only .206 %

30 minutes	after	50 gms	of	Glucose	-	.312 %
90	"	"	"	"	"	- .256 %
150	"	"	"	"	"	- .212 %

Thus comparing very favourably with the previous test (see chart).

I also tried the effect on the urine of injecting 1cc. of Insulin or 20 units, twice a day for 2 days; but as the patient complained of dizziness, occasional faintness and sweating, I have resumed the 10 units dose under which he says he feels much more comfortable.

These symptoms indicated a state of Hypoglycaemia, which must be carefully avoided. The urine after the increased injections showed only a trace of sugar, but the sugar reaction was never absent. In this case I propose to continue the 10 unit dose of Insulin, and restrict diet for some time, in the hope that the Islets of Langerhans may recover their Endocrinous activity.

CASE 4.

A. S. aged 52, Tailor.

Height 5ft 4ins

Weight 9st 3lbs.

This man first consulted me in April 1923 on account of intense thirst, weakness, and loss of

CASE 4 contd.

flesh. On examination I found his heart normal, chronic bronchitis present, and severe pyorrhoea alveolaris.

Urine.

Amount	8 pints.
Sp. gr.	1030
Sugar	3 %
Acetone and Diacetic acid	present
Albumin	none.

I advised this patient to stop his work, and undergo the "Allen" treatment, but as his circumstances would not permit of this, I put him on the restricted diet detailed above with instructions to have his teeth attended to. After three months dietetic treatment, the sugar fell to 1.5 % but acetone and diacetic acid were still present.

I then prevailed on him to carry out the starvation treatment, and after a fortnight the urine was free from sugar, acetone and diacetic acid, but as soon as the original Restricted Diet was resorted to sugar appeared in the urine to the extent of 1 % but this time without acetone or diacetic acid.

I accordingly decided to try Insulin. In the first place I made a blood sugar analysis with the following result:-

Initial	-	.112 %
30 minutes after 50 gms of Glucose	-	.243 %
90 " " " " " "	-	.187 %
150 " " " " " "	-	.156 %

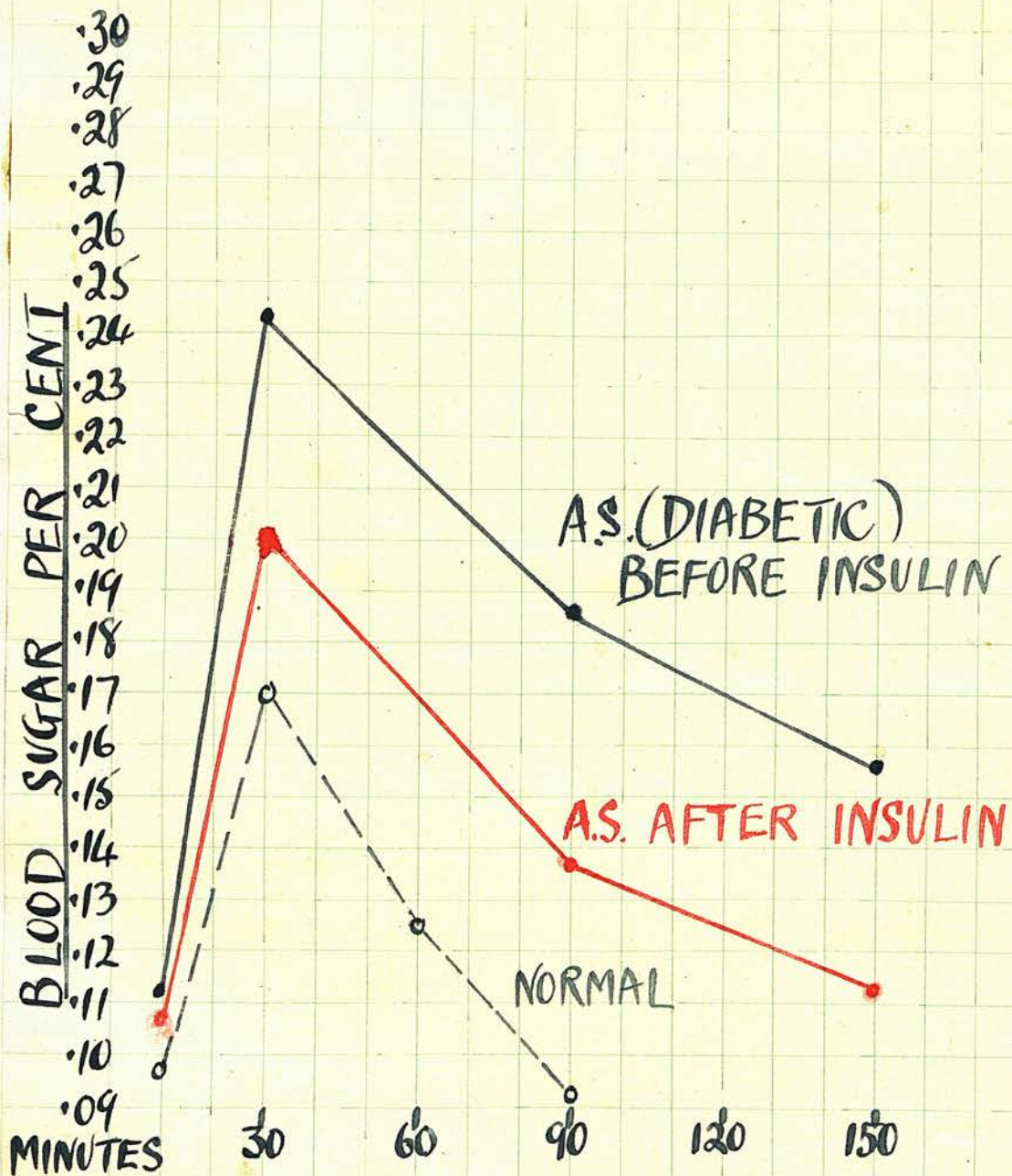
CASE 44 contd.

These figures pointed to the patient being a true diabetic, the sugar rising high, and failing to drop to the original even after $2\frac{1}{2}$ hours. The patient was kept on the same Restricted Diet and given 5 units (.25cc.) of Insulin twice a day $\frac{1}{2}$ an hour before food. The result in this case was dramatic; after 4 injections there was no sugar, acetone or diacetic acid. The patient said he felt very much better, and his intense thirst and weakness disappeared. This case was interesting in that shortly after the first two Insulin injections he complained of a gnawing pain in the abdomen at the level of the umbilicus which however ceased a few hours afterwards.

Insulin was given for a week, during which time the urine was examined daily and no sugar found. Insulin was then stopped for a week and the urine examined daily, and sugar still remained absent. A fortnight after the commencement of the Insulin treatment another blood sugar test was made with this result:-

Initial	-	.106 %
30 minutes after 50 gms of Glucose	-	.200 %
90 " " " " " "	-	.137 %
150 " " " " " "	-	.112 %

The patient is now getting 5 units (.25cc.) twice a day, and is feeling quite fit. (see chart).

CHART 4.

Case 5: Mrs. F. aged 50, height 5ft. weight 9st 2 lbs. has been under my care for about 12 months.

When she was first examined in September 1922 the urine contained 2% of glucose but no acetone or diacetic acid. After a month's careful dieting, and occasional fasting, the glucose rapidly decreased until at the beginning of November 1922 there was no sugar. Heart, Lungs and Kidneys healthy. Since then the urine has been examined every month, and traces of sugar discovered. The patient's chief complaints have been thirst and lassitude.

I made a blood-sugar analysis for sugar in August 1923 using Maclean's method with the following result:

On a fasting stomach I found the urine free from sugar, and the blood-sugar .12%, which is above the normal; normally it should be .09 to .1. I then gave her 50 grams of Glucose with the following results,

In 30 minutes	Blood-sugar	-	.202
" 90	" " "	-	.237
" 150	" " "	-	.181

Now the urine was found to be loaded with sugar. These figures indicate a true Pancreatic Diabetes

In a normal subject or even in Glycosuria the blood-sugar should not rise above .18%, and should return to normal in from $1\frac{1}{2}$ to 2 hours which it did not.

In my opinion this is a mild case of Diabetes. I put this patient on the following diet, and gave her 5 units of Insulin twice a day, half an hour before

Case 5 contd.

meals. v'3:-

Breakfast: Coffee with $\frac{1}{2}$ oz milk, 1 egg, 1oz butter
1 oz brown bread, 4 ozs. lettuce or other
salad.

Dinner: Beef Tea, 4 ozs Cod or Haddock, 1 Bran
Biscuit, 1 oz butter, 5 oz celery,
 $\frac{1}{2}$ oz salad oil.

Tea: Tea with $\frac{1}{2}$ oz milk, 1oz brown bread, $\frac{1}{2}$ oz
butter, 1 egg.

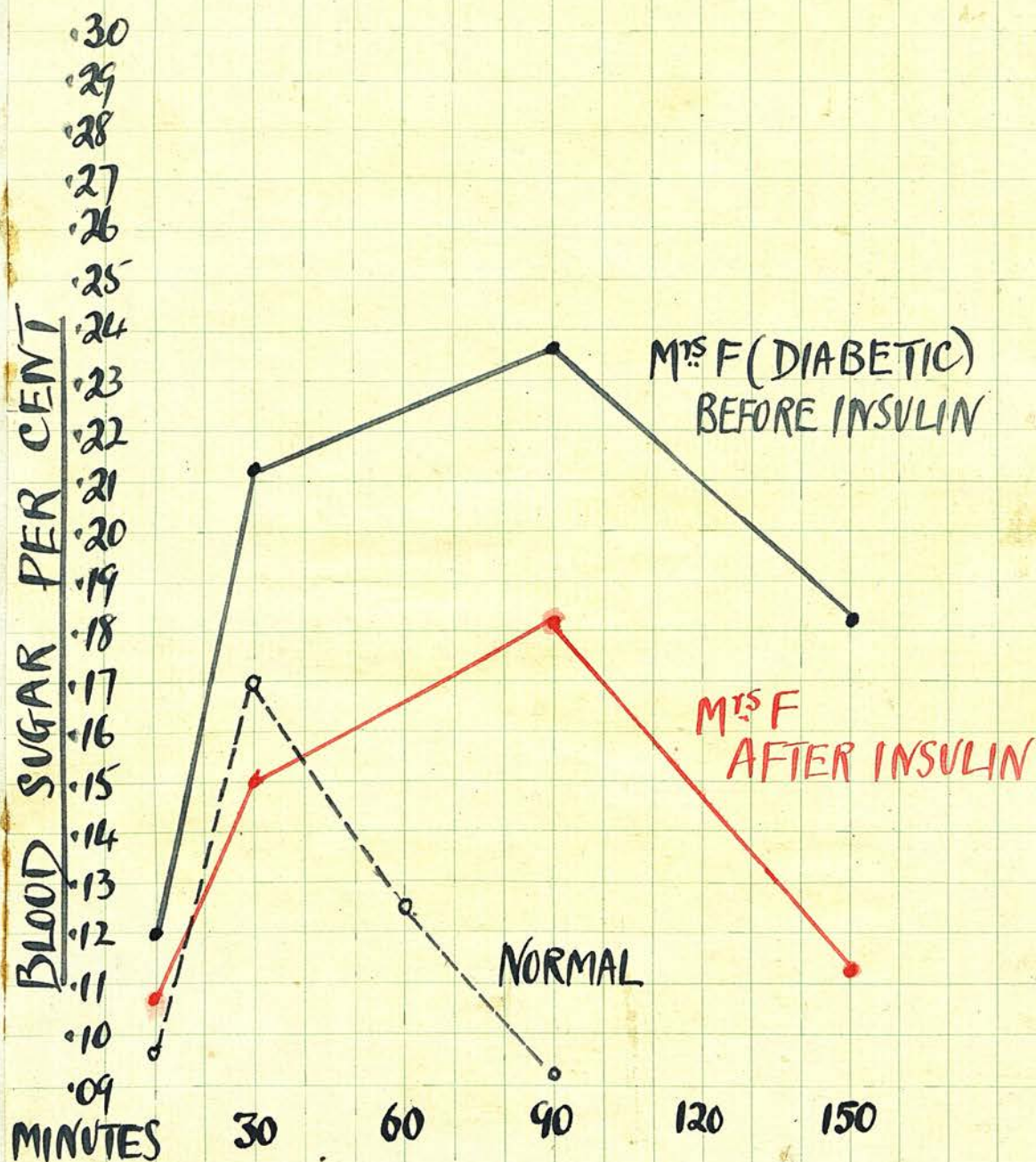
Supper: Beef Tea, 3ozs chicken, 3ozs potatoes,
5ozs watercress etc. $\frac{1}{2}$ oz salad oil.

At the end of a fortnight's treatment, a
blood-sugar analysis was made with the following
result:-

Initial	.106%
30 minutes after 50 grams of glucose	- .150%
90 " " " " " "	- .181%
150 " " " " " "	- .112%

From chart 5, it will be seen that after
Insulin the initial reading is normal, the highest
level is below .19% and blood-sugar percentage becomes
practically normal in $2\frac{1}{2}$ hours. The Insulin was now
stopped and the patient advised to continue the above
diet for a month with a weekly fast day. At the end of
a month there was no sugar in the urine, the blood-
sugar was .106%, and the patient states she feels
very fit.

33.
CHART 5.



CASE 6

M.A. aged 59, Traveller.

Height 5ft 4ins. Weight 11st. 13lbs.

This man first consulted me in July 1923 for
thirst, weakness and recurring boils.

Heart and Lungs normal.

Urine

Amount 7 pints.

Sp. gr. 1040

Sugar 2 per cent.

Acetone and Diacetic Acid both present

Albumin none

He was put on the Restricted Diet* for a week,
and then on Starvation treatment. After two fasts of
48 hours the urine became sugar free, but on the
resumption of the Restricted Diet sugar appeared in
the urine to the extent of 1 per cent.

Blood sugar tests were carried out 24 hours
before and 24 hours after Starvation treatment with
the following results:-

Before "Allen" Treatment.

Initial	-	.187 %
30 minutes after 50 gms. of Glucose	-	.256 %
90 " " " " "	-	.225 %
150 " " " " "	-	.200 %

After "Allen" Treatment.

Initial	-	.118 %
30 minutes after 50 gms. of Glucose	-	.175 %
90 " " " " "	-	.131 %
150 " " " " "	-	.125 %

CASE 6 contd.

When the blood analyses were carried out, the patient was on Restricted Diet ^{*} at the time.

I now decided to try the effect of Insulin after the "Allen" treatment, and obtained the following result:-

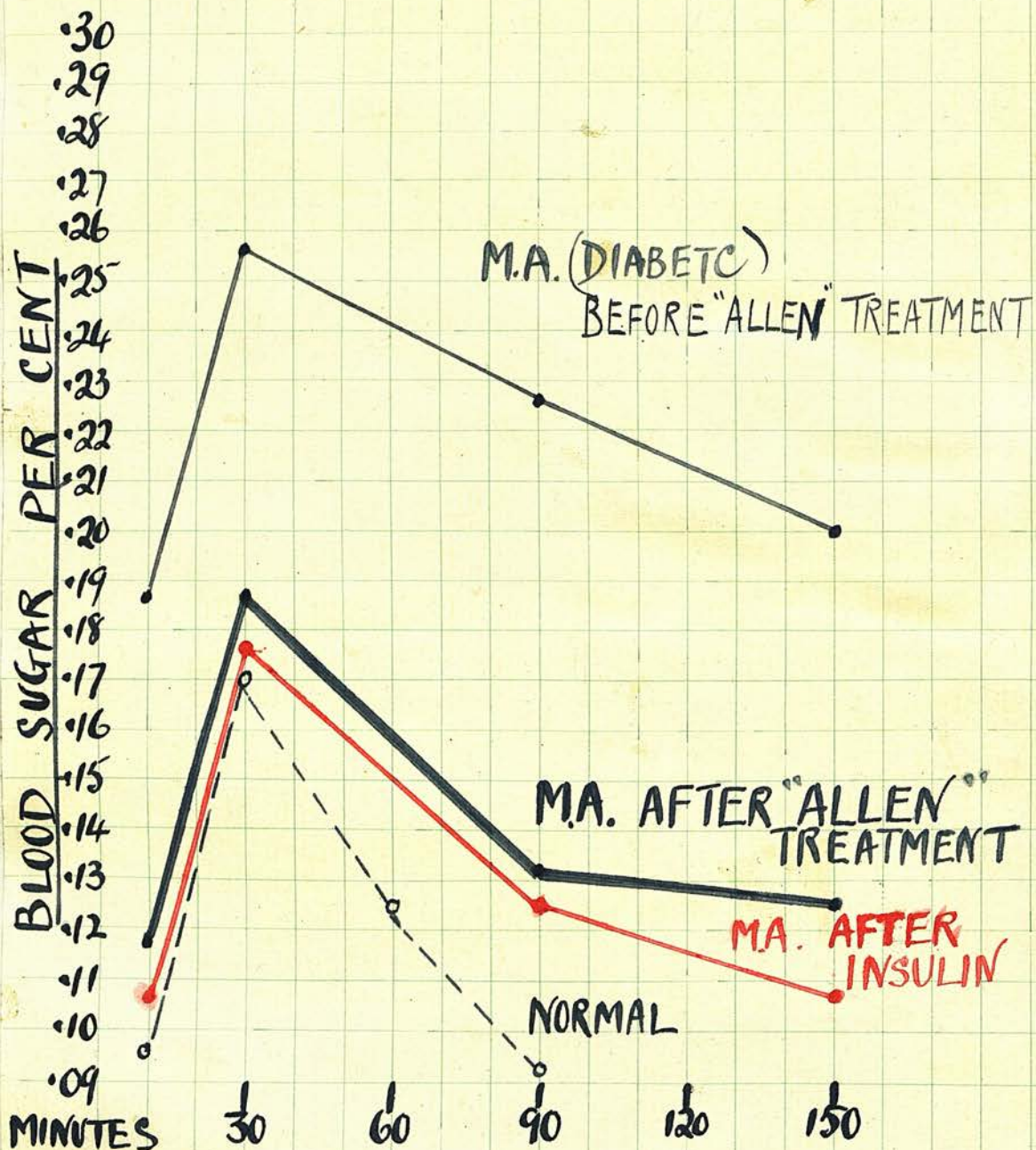
10 units (5cc.) of Insulin were injected $\frac{1}{2}$ an hour before food, twice a day for a week whilst the patient was on the same Restricted Diet. The urine became sugar free on the 3rd. day and remained so.

A Blood analysis was made at the end of the week.

Initial Sugar	-	.106 %
30 mins. after 50 gms. of Glucose	-	.175 %
90 " " " " " "	-	.125 %
150 " " " " " "	-	.106 %

These figures show that not only did Insulin reduce the percentage of blood sugar, but also that the storage capacity was considerably enhanced. The sugar tolerance curve as will be seen from the chart approximates closely to the normal.

CHART 6.



(3). CLASSIFICATION OF THE VARIOUS KINDS
OF TREATMENT.

In connection with the treatment of Diabetes we have to consider (a) Dietetic (b) Drugs (c) Insulin treatment.

(a). Dietetic.

Let us first consider Von Noorden's views on this subject, as they were accepted for many years as constituting a rational method for combating this disorder of metabolism. (See Von Noorden's "Diabetes Mellitus" p 190 1907).

Von Noorden is of the opinion that obesity is an early symptom of the diabetic condition and that it develops long before glucose makes its appearance in the urine. Von Noorden considers it desirable to adopt a prophylactic treatment in the case of those persons who are known to have a hereditary tendency to this disease. It has been advised that the capacity of such individuals to store up carbohydrates should be tested. This may be done by giving 100 grams of glucose on an empty stomach, if this causes glycosuria it may be inferred that this capacity is abnormally low as a normal person should be able to take 180 to 250 grams without becoming glycosuric. In such cases the intake of carbohydrates should be restricted, and by this means Von Noorden thinks the development of Diabetes may be prevented.

Von Noorden devised a test diet to determine the severity of the diabetes.

Breakfast: 200 grammes (8ozs) of tea or coffee with
1 or 2 tablespoonfuls of thick cream,
100 grammes (4ozs) of cooked meat,
Butter, 2 eggs with bacon,
50 grammes (2ozs) of white bread.

Lunch: 2 cooked eggs, cooked meat 200 to 250
grammes (8-10ozs)
Vegetables (Spinach, cabbage, cauliflower
asparagus with sauce for gravy without
flour, but with butter, eggs, etc.
Creamy cheese (Cainembert Brie etc.) 20
to 25 grammes (about 1 oz) plenty of
butter, 2 glasses of red or white wine if
desired, 1 small cup of coffee with a
tablespoonful or two of thick cream, 50
grammes (2ozs) of white bread.

Dinner: Clear meat soup with egg or green vege-
table in it, Meat as at lunch, Vegetables
as at lunch, Salad of lettuce , cucumber
or tomatoes, Wine, (no bread).

Beverage during the day (exclusive of wines) one or
two bottles of Apollinaris or Seltzer water.

If on this diet no sugar appears in the urine,
the quantity of bread is gradually increased until
sugar does appear in the urine, the diet is maintained
till the daily quantity of sugar excreted has become
nearly constant. Then the quantity of bread is gradual-
ly diminished until the urine becomes free from sugar
while there is yet bread in the daily fare, in which
case we have to do with a slight form of diabetes,

Von Noorden's test diet contd.

and we learn also the tolerating capacity of the patient for carbohydrates.

This capacity will be found to vary greatly and will determine the particular diet suited to each individual. If however we find that with this test diet the urine does not become free from sugar until bread is totally excluded, then we know we have to do with a severe form of diabetes. In other cases even the total exclusion of bread does not prevent the appearance of sugar in the urine, and the proteins have to be reduced before the urine becomes sugar free.

Von Noorden classifies the two latter forms as moderately severe and severe cases, and he terms most extreme cases those which continue to pass sugar in the urine even with a total exclusion of carbohydrates from the diet together with a reduction of proteins.

Having by means of a test diet determined the form and severity of the case with which we have to deal we are in a position to prescribe a suitable dietary remembering the principles already laid down.

If in intermediate or moderately severe forms we can by diet keep the excretion of sugar at or below 500 grains a day and at the same time maintain the patient's weight and strength there is little need for drugs, but when we fail to do this it may be desirable to have recourse to their aid.

Oatmeal was strongly advocated by Von Noorden

Von Noorden's test diet contd.

as giving remarkably good results in certain cases. "The "oat cure" he says "as now prescribed by me consists in the daily administration of 200 to 250 grammes of oatmeal best given in the form of gruel every 2 hours, 200 to 300 grammes of butter and often about 100 grammes of vegetable proteid or a few eggs may be taken addition. Otherwise nothing else is allowed except black coffee or tea, lemon juice, good old wine or a little brandy or whisky.

" The oat-cure rendered me immense service in severe cases and I may even say that I have often succeeded in fending off incipient coma by its use. One should under no circumstances allow other carbohydrate to be taken at the same time as the oatmeal".

Before attempting the "oat-cure" it is important to reduce the glycosuria as low as possible by the usual dietetic methods. Von Noorden never orders more than three oatmeal days in succession, then a day of vegetable proteins or a partial fast day, prior to a further three days of the "oat-cure". He recommends Klopfer's "glidine" as the best of the vegetable protein preparations. He speaks well also of the "potato cure". He says " I have thoroughly tested Mosse's statements and can confirm the fact that with due attention to the principles laid down by him, potatoes can be much better tolerated than would be supposed from the amount of carbohydrates they contain".

Von Noorden recommended weekly fast days which he called "Diabetic Sundays", and pointed out that the good effects of a fast day contained many days

beyond the actual fast.

The Modern treatment of diabetes resolves itself into the management of ~~the~~ mild cases ~~and~~ severe cases.

Treatment of mild cases of diabetes, can according to Joslin¹² be carried out in various ways. For instance one method is to decrease the total quantity of the diet, regardless of the constituents until a slight loss of weight is brought about. Sometimes this is all that is required to render the urine sugar free. In other cases the sugar and starchy food may be withdrawn from the diet, and this procedure may bring about the same successful result. The drawback to such a plan, however is the production of acid poisoning, owing to the omission of so much carbohydrate food without the simultaneous omission of fat. It is therefore desirable and advisable to follow some definite system of curtailing the diet and know exactly the caloric value of the foodstuffs consumed.

Joslin¹ recommends giving a Test Diet and calculating the heat value of the Carbohydrate, protein and fat.

Test Diet for Diabetic Weighing 90 Kilos - 198lbs.

Food	Quantity	Carbohydrate	Protein	Fat.
Orange	3 (300grams)	30	0	0
Shredded Wheat	1 piece	23	3	0
Milk	480cc (16ozs)	24	16	16
Fish	120gm (4ozs)	0	24	0
Meat	150gm (5ozs)	0	40	25
5%Vegetables	300gm (10ozs)	10	5	0
Potato	240gm (8ozs)	48	8	0

Test Diet for Diabetic Weighing 90 Kilos - 198lbs cond

Food	Quantity	Carbohydrate	Protein	Fat
Bread	180gm (6ozs)	108	18	0
		<u>243gm</u>	<u>114gm</u>	<u>41gm</u>
		4	4	9
	Calories	<u>972</u>	<u>456</u>	<u>369</u>
	Total	<u>1797</u>		

The above diet would be modified according to the amount of sugar in the urine, sugar in the blood, patients work and environment.

Treatment of severe cases.

The treatment of such cases has been attended with excellent results, and consists in Fasting i.e. the Starvation or Allen treatment.

The method is as follows:-

Fast four days, unless earlier sugar free. Allow water freely, tea, coffee, and thin clear meat broths as desired. If glycosuria persists at the end of 4 days give 1 gram protein or 0.5 gram Carbohydrate per Kilo body weight for 2 days, then fast again for three days unless earlier sugar free. If glycosuria remains repeat and then fast for 1 or 2 days as necessary. If there is still sugar, give proteins as before for 4 days, then fast 1 day and then gradually increase the periods of feeding, one day each time until fasting one day each week.

Carbohydrate Tolerance.

When the 24 hour urine is free from sugar give 5-10grams Carbohydrate (150-300 grams of 5% vegetables) and continue to add 5-10 gms Carbohydrate daily up to 50 grams or more until sugar appears then fast until sugar free.

Protein Tolerance.

When the urine is again sugar-free decrease the carbohydrate tolerance or at least 10 grams and then add about 20 grams protein, and after that 15 gms protein daily in the form of egg-white, fish or lean meat(chicken) until the patient is receiving from 1-1.5 grams protein per Kilogram body weight.

Fat Tolerance.

It is usually desirable especially in the young to add no fat until the protein reaches 1-1.5 grams protein per Kilogram body weight, and the blood sugar is normal. Then add 5-25 grams daily according to previous acidosis until the patient ceases to lose weight or receives in the total diet 20-30 calories per Kilogram body weight.

Reappearance of sugar.

The return of sugar demands fasting for 24 hours or until sugar-free. Resume the former diet, adding fat gradually, and last of all in order to maintain as high a carbohydrate tolerance as possible sacrificing body weight for this purpose.

Weekly Fast Days.

Whether sugar reappears in the urine or not, it is desirable upon one day each week to rest that function of the body which controls the assimilation of sugar by either a complete fast day or a diet of low caloric value.

Whenever this tolerance is less than 20 grams cut the diet in half one day each week (half-day).

Number of Calories Required.

This is found to vary with circumstances, habits, work etc. Whereas a patient who is resting quietly can manage with only 20 calories per Kilo body weight per day generally a minimum of 25 - 30 calories per Kilo is required by the average individual.

When a diet has been found which is sufficient for the patient's needs without glycosuria he may continue steadily with it. Generally speaking the patient is advised to eat less rather than more.

The Allen treatment of Diabetes has led to an enormous reduction in the death rate. Thus whereas the mortality in Massachusetts General Hospital between 1898 and 1914 was 28%, in 1918 it was only 4%.

Beverages.

Sweet wines or aerated waters containing sugar must not be taken. The value of alcohol in diabetes is questionable. When a patient however is on low diet, a little dry sherry, or diluted brandy or whisky, may aid the digestion of the meals and does not cause an increase of sugar in the urine.

Hygiene.

The care of the mouth and teeth, attention to the bowels, and daily warm baths, are of the utmost importance. Auto-intoxication must be eliminated as far as possible. Diabetics must avoid worry and emotional excitement, have moderate exercise, and plenty of rest. Warm clothing is desirable to prevent heat waste. General massage is often beneficial where the patient

Hygiene contd.

cannot have active exercise.

Drugs.

These are practically obsolete now, and should be avoided as far as possible except in the relief of special distressing symptoms. The regular administration of Opium, Codeia etc., is to be condemned. Mild laxatives may be required occasionally, and arsenic and iron if the patient is anaemic.

Insulin Treatment.

In the first place a diet based upon the normal basal calorie requirement for the age height weight and sex of the patient is calculated. This diet contains sufficient protein to maintain nitrogenous equilibrium and carbohydrates and fats in such a proportion as to prevent the excessive production of acetone and diacetic acid.

It is often advisable to make the patient fast a day or so in order to bring the sugar excretion to a constant level more quickly. The patient is kept in bed at first and afterwards only light exercise is allowed.

In hospital examinations of the blood and urine are carried out daily for about a week or more but in private practice this is not practicable.

At the end of this period, if the patient shows decided glycosuria and hyperglycaemia, and especially if acidosis is present, Insulin is given. The diet is divided into two large meals in which practically all the Carbohydrate is taken and two small meals containing little or no carbohydrate and only a few calories.

The patient must be warned that unpleasant sensations may follow the Insulin injections and should always have some sugar or barley sugar with him, which he can eat when these come on.

10 units of Insulin are injected subcutaneously about half an hour before the large meals. Collect the 24 hours' urine and examine it for sugar. This dose

Insulin Treatment contd.

is continued for three days when if the urine still contains sugar, 15 units of Insulin may be injected. If after three more days of this treatment glycosuria is still present the dose may be increased to 20 units in the morning followed by 15 units in the evening. If glycosuria persists after a few days of this dosage, 20 units may be given twice a day. If glycosuria now disappears the dose is approximately correct for the diet, but unless the percentage of blood sugar is determined, it will be safer to reduce the dose to 15 units in the morning and 15 units at night.

This may be continued for a long period provided the same diet is adhered to. If the diet is considered insufficient, a little more carbohydrate may be added to the two larger meals, and if this produces glycosuria the dose of Insulin may be gradually increased in order to ascertain what amount will cause a trace of sugar to appear in the urine.

The treatment should be controlled from time to time by blood-sugar tests. If these cannot be carried out, it is ~~is~~ inadvisable to exceed a dose of 20 units twice a day; at all events the dose should only be increased cautiously.

In addition to the quantitative estimation of sugar in the urine and in the blood, there are other methods of investigating the metabolic state of the individual. These include the determination of CO₂ combining power of the blood.

Insulin Treatment contd.

(Van Slyke's method), alveolar air CO_2 (Marriott's method); basal metabolism and respiratory quotients (Douglas Haldane and Tissot Haldane), total nitrogen in the urine (Kjeldahl).

Generally speaking however, a careful study of the sugar in the urine, and blood, and presence or absence of acetone and diacetic acid is the essential requirement in the correct treatment of a case.

According to Banting one unit of Insulin might be regarded as metabolizing 2 - $2\frac{1}{2}$ grains of carbohydrate in a severe case, whilst in a mild case 5 - 6 grains might be metabolized. He advised not more than 5 units to begin with unless the patient is comatose and only one dose daily to be given, an hour before meals.

The patient should be kept sugar-free by dieting and Insulin; when sugar-free the pancreas tended to produce Insulin.

It was necessary to keep the blood-sugar within normal limits, as Allen's experiments on diabetic dogs had shown that overworking of the B- cells of the islets of Langerhans by doses of sugar caused degeneration of these cells.

Reactions and Hypoglycaemia.

With the exception of possible urticarial eruptions in a sensitive patient, no toxic effects due to split protein products occur, as the present Insulin is practically protein free.

Insulin administration may however be followed by a condition of Hypoglycaemia in which the sugar in the blood may fall to an abnormally low level.

Insulin Treatment.contd.

The symptoms complained of are weakness, anxiety, dizziness, visual disturbances and profuse sweating. The severity of these symptoms increases with the hypoglycaemia. When the blood-sugar is about .07% the patient begins to experience these sensations.

If the blood-sugar falls below .05% the patient may become comatose with hypotonia and loss of deep reflexes. The symptoms can be easily counteracted by the administration of glucose, sugar or fruit juice.

I have now treated 4 cases with Insulin and have carried out regular urinary analysis and blood-sugar estimations, and at the same time had the opportunity of watching the cases closely from a clinical point of view.

In the case of Mr. M, Special Restricted Diet reduced the amount of sugar in the urine from 5% to 3.5%, but Ketonuria always remained. On the other hand when 10 units of Insulin were injected, and the same Restricted Diet adhered to the clinical picture was quite altered.

On the 4th day of Insulin treatment the percentage of sugar in the urine fell to 1.5%, and Ketonuria had disappeared. At the end of a week the patient who had hitherto been languid listless and low-spirited, became bright and buoyant. He would keep on saying " he never felt better in his life", and his cheerful countenance confirmed his statement. Not only did the patient's subjective condition improve

Insulin Treatment contd.

greatly, but the blood-sugar estimation at the end of a fortnight's Insulin treatment showed considerable diminution in the percentage of blood-sugar viz .206% as compared with .312% before the treatment.

The sugar tolerance curve also shows less prolongation after Insulin, thus indicating better storage capacity. Besides, the condition of acidosis which existed for months was eliminated.

In the case of A.S, I observed the effects of the Special Restricted Diet, followed by the Allen treatment, and lastly Insulin.

Under the Restricted Diet sugar fell from 3% to 1.5% but Ketonuria still persisted. Under the Allen treatment, the urine was free from sugar and Ketones, but on the resumption of the Restricted Diet, the patient again developed Glycosuria but no Ketonuria.

After 4 injections of 5 units of Insulin (.25cc) however, sugar disappeared from the urine, and remained absent, even a week after Insulin was discontinued. The blood-sugar after Insulin was .106 as compared with .112 before Insulin, and the sugar tolerance curve after Insulin approximates more closely to the normal (see Chart)

There can be no doubt that the Insulin treatment produced more lasting benefit in this case than the Allen treatment.

The Case of M.A.

The Case of M.A. affords an interesting comparison between the percentage of blood-sugar after the "Allen" treatment alone, and that following the Allen treatment + Insulin.

Whilst the "Allen" treatment rendered the urine sugar-free after two fasts of 48 hours each, glycosuria reappeared when the patient was put on Restricted Diet; on the other hand after the Insulin the urine remained sugar-free, with the same Diet.

The "Allen" treatment must be credited in this case with having reduced the blood-sugar to a considerable degree, but the aid of Insulin was evidently required to reduce it still further. Besides the Sugar tolerance Curve after Insulin is practically a normal curve, the level not rising to .18%, the sugar storage being effective, and the percentage falling to the initial reading.

Treatment of Complications.Skin.

Pruritus of the skin and genital organs is often a very distressing symptoms, and makes the patient extremely miserable.

Frequent sponging of the body with tepid water, and the wearing of some absorbent material such as thin flannel, and frequently changed, are advisable.

Lotions are often useful

Rx.

Sodii Hyposulphit	$\frac{1}{2}$ oz.
Aqua	6ozs.



Treatment of Complications contd.

or

Acid Hydrocyan Dil 1dr.

Glycerin 1oz.

Aqua ad 6ozs.

The genital organs should be kept scrupulously clean and cotton wool applied immediately after micturition.

Respiratory System

Diabetics are particularly susceptible to Phthisis, they must therefore be warned against contracting cold, which would predispose to the latter condition.

Urinary System.

Albuminuria occurs frequently; but it is often slight. Attention to the skin and bowels is of the utmost importance.

Special Senses - Cataract & Diabetic Retinitis

The former generally requires operation.

Nervous System.

Neuritis, especially of the lower limbs is very common. Massage and electrical treatment may be employed. The most rational method is to improve the sugar-metabolism.

Coma, is the most serious complication of Diabetes, and is the most frequent cause of death. The original determining cause is acidosis. To combat acidosis and prevent the onset of coma must ever be the duty of the physician. Frequent examination of the urine as to the presence of Acetone and diacetic acid must be carried out regularly.

In addition the patient must be warned against the following predisposing causes of Coma:-

- 1) Physical fatigue
- 2) Traumata
- 3) Violent Emotion, worry and grief.
- 4) Infectious Diseases, influenza, pneumonia etc.

The diabetic should avoid visiting infectious patients.

- 5) Surgical operations, especially under chloroform.
- 6) Sudden increase in diet and deprivation of Carbohydrates!

Treatment of Coma contd.

Keep the patient quietly in bed, as warm and as comfortable as possible.

Clear the bowels out thoroughly by enemata and purgatives. It is also advisable to empty the stomach by pump, especially if full of food or distended.

If the patient is fasting, give only Carbohydrate and protein; if on ordinary diet stop the fat and give carbohydrate and protein for one day, then fast. Sometimes it is best to fast at once. Large amounts of warm fluid should be given to flush out the system. 2 pints may be given in the first four hours, then the quantity is reduced. Tea, Coffee and Water are best. Coffee and brandy may be given by rectum. In threatening heart failure subcutaneous injection of Camphor gr. $3\frac{1}{2}$ in loc. of oil should be tried, also Digitalin.

The subcutaneous injection of laevulose 10% has been recommended in fasting cases. Large quantities of Bicarbonate of Soda intravenously were at one time strongly advocated, but now such treatment is not recommended. Joslin deprecates its use.

Treatment of Coma by Insulin.

Although I see a large number of cases of Diabetes in my Jewish practice in Glasgow, I do not recollect having seen a case of Coma for the past two years, so have not had the opportunity of testing Insulin in this condition.

According to Banting, Campbell and Fletcher,

Treatment of Coma by Insulin contd.

Insulin is a specific in the treatment of Diabetic Coma, and they report 10 cases in which 6 recovered. It is administered either subcutaneously, or intravenously followed by subcutaneous injections. The dose is far in excess of the requirement, but the danger of Hypoglycaemia is obviated by the administration of Glucose at the same time.

From the reports of these and other authorities, it seems that Insulin is so far the most powerful weapon we have for the treatment of Diabetic Coma.

Summary.

1. Diabetes is a state of Overburdened Carbohydrate Proteid and Fat Metabolism.
2. The Modern treatment dates back to the Epoch making discoveries of Merling and Minkowski in 1889 regarding the function of the pancreas. The General Metabolism in Diabetes was closely studied by Von Noorden, who recommended special test diets to determine the severity of the Diabetes.
3. Latterly the experimental work of Dr. F.M. Allen put the dietetic treatment on a sound scientific bases. He showed 1) that there was deficient functioning of the islets of Langerhans in Diabetes, and 2) that starvation treatment could control the disease.
4. As precursors of the Insulin treatment we must mention the pancreatic extracts used by Zuelzer who by intravenous injection succeeded in reducing

Summary contd.

Glycosuria in several cases.

5. Lastly, Banting and Best's discovery of Insulin mark the climax of recent researches in the rational treatment of Diabetes.

Dietetic Treatment.

6. The "Allen" method of starvation is the dietetic treatment par excellence.

I have observed uniformly good results in my own practice; the drawback is the necessity for the patient to give up his employment for a while.

-
7. Drugs are practically valueless.

8. Insulin seems so far to be very efficacious in controlling the disease; but to what extent it may be curative can only be determined in the future. My own cases have made wonderful progress, and they all manifest a feeling of satisfaction with the treatment.

9. The Insulin treatment is more suitable for workers than the "Allen" treatment, as the patients can carry on their occupation if not too strenuous.

10. Blood-sugar estimations are an excellent gauge for determining the real progress of the case.

11. Insulin seems to reduce the blood-sugar for a longer period than the "Allen" treatment, and the sugar tolerance curve becomes practically normal.
-

12. Insulin is claimed to be a Specific in Diabetic Coma.

13. The dosage of Insulin must be carefully studied in order to steer a clear course between the Scylla of Hyperglycaemia and the Charybdis of Hypoglycaemia.

All my cases were Jewish patients.

Knowing the prevalence of Diabetes amongst Jews, I have reflected on its probable causation. In the cases I have described, and those I have observed in addition, I find that they practically all take a large amount of bread with their meals. Non-Jews on the other hand take more potatoes with their principal meal.

	Carbohydrate	Protein	Fat
* Now 1oz. of Bread contains	15	2	0 grams
1oz. " Potato "	6	0.5	0

it will be seen that there is a preponderance of 9 grams of Carbohydrate in bread over potato, per ounce.

The neurotic temperament which is so common in my race has doubtless a determining influence in the production of this disorder of metabolism.

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I. H. Hipelz
M.B.Ch.B.